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REMARKS

Claims 26-28 are currently pending in the application. By this amendment, claims 1-25 are cancelled without prejudice, being directed to a non-elected invention, and claim 26 is amended for the Examiner's consideration. The foregoing separate sheets marked as "Listing of Claims" show all the claims in the application, with an indication of the current status of each.

Claim 26 has been amended to recite "A method *to treat* signs of aging...". This amendment was carried out to correct the previous lack of antecedent basis for "the treatment" in line 1. Support for this language is found, for example, on page 8 at line 14. Claim 26 has also been amended to recite that the method comprises administering an effective amount of a composition comprising one or more rhamnolipids to "a subject in need of *a treatment for signs of aging of the skin*". This amendment has been made in order to clarify the subject matter of the invention, i.e. the method is for subjects needing treatment for signs of aging of the skin, and not for any other indication. In so doing, Applicant has replaced "thereof" with the phrase to which it referred (treatment for signs of aging of the skin). No new matter has been added to the claim by these amendments.

The Examiner has rejected claims 26-28 under 35 U.S.C. §102(a) as being anticipated by U.S. Patent No. 5,455,232 to Piljac et al. ("Piljac '232") or U.S. Patent No. 5,466,675 to Piljac et al. ("Piljac '675"). These prior art references have an inventor, Goran Piljac, in common with the present invention. There are certain additional disclosures in the present invention, and additional claims. In principle, the issue is whether the new claims are novel and non-obvious over the prior inventions, in view of the additional disclosures.

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The Examiner notes that the formulation of rhamnolipid described in the present invention is the same as that described in these two prior art references. The Examiner concedes that the references are silent regarding treatment of "signs of aging", but makes the following argument. As to Piljac '232, since the patients are not identified as infants the topical application of the rhamnolipid described in the reference must necessarily treat signs of aging. Essentially the same argument is made as to Piljac '675. In short, the prior disclosed application of the rhamnolipid to the skin necessarily is a disclosure of use of the rhamnolipid to treat signs of aging, since some signs of aging must be presumed.

This is threadbare argument that does not withstand scrutiny. Under this argument, it makes no difference whether signs of aging are observable or not. A young adult in prime physical condition, or a young person not yet fully grown, would not appropriately be assumed to show signs of aging. Yet the logic of the Examiner sweeps in these groups of individuals. The Examiner's logic is purely chronological: as one ages, there must necessarily be signs of aging. If this logic is taken at face value, it would also include infants themselves, who by this logic begin to "age" from birth. It will also be observed that the language of the amended claim limits application to "a subject in need of treatment for signs of aging of the skin", not simply to anyone presumed (by virtue of not being an infant) to have signs of aging.

The Examiner includes freckling and pigmentation in his list of conditions which the Examiner, apparently, associates with "signs of aging". But the Examiner's list is not the list of the inventors. The inventors only provide one example, "wrinkles" (page 8, line14). It should be noted that the other examples on the Examiner's list are dubious. Freckles are common in children and pigmentation is an ordinary attribute of skin color. The Examiner includes dryness and roughness in his

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list of conditions, but both these may be caused by wear and tear other than aging.
“Sun damage”, on its face, applies to overexposure not necessarily related to age.

For a suitable indication of “signs of aging” it makes more sense to look first to the observations of the inventors, and what they said in the specification. It must be presumed that it is the content of the specification that is the basis for the conclusion of the inventors that the rhamnolipids of interest (described in both the Piljac references and the present invention) serve to provide “a cosmetic composition ... in an amount effective to treat signs of aging, such as wrinkles” (page 8, lines 12-14).

The disclosure of the present invention is quite different from the disclosures of Piljac ‘232 and Piljac ‘675. Piljac ‘232 describes how the rhamnolipid is made and then summarily refers to “extensive research” showing a “curing action on dermatological diseases, such as Acnae vulgaris, Pytiriasis versicolor, ...” and a long list of other such conditions (col. 1, lines 20-39). The disclosure also indicates that the concentration of active rhamnolipid ingredient depends “on the disease to be treated, ...the seriousness of the disease, the age of the patient, and the like” (col. 4, lines 18-20). Further, it is indicated that human patients were treated for four specific diseases, and that the features of these diseases disappeared after two weeks (col. 5, lines 32-35).

Piljac ‘675 contains a more extensive disclosure, addressed to the treatment of autoimmune diseases. A background section describes the immune response, autoimmune diseases, including organ specific autoimmune diseases, AIDS, and certain other diseases believed to be related to the neuro-immune system. The disclosure shows how the rhamnolipid is made (cols. 8-15), and then gives results for in vitro tests (cols. 15-20) and in-vivo tests (cols. 21-28). The in-vitro tests included tests against enzymes, viruses, certain bacteria, and tests on cell cytotoxicity,

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hemolytic activity, and lymphocyte proliferation. The in-vivo test involve stimulation and suppression of the immune system, restoration of the immune system, and tests for chromosomal aberrations and toxic effects. A final part of the disclosure described concerned clinical results of treatments on human patients for psoriasis.

By contrast, the present invention is concerned neither with disease conditions nor the immune system, but rather with re-epithelization processes. As the Examiner recognized, the disclosure noted the striking difference with respect to the formation of scar tissue between adult injury to skin tissue and wounds to fetuses. The disclosure describes aspects of the response to wounds, including elevated levels of hyaluronic acid (page 2, lines 12-14), the adhesion of glycoproteins (page 2, lines 18-20), and the effects of slow acting macrophage-derived cytokines and chemokines (page 2, lines 27-31) on the replacement of differentiated tissues by fibrous tissues (page 3, lines 4-8). At the conclusion of this background discussion the disclosure points to the "need to develop methods for inducing re-epithelization in adult skin tissue" (page 3, lines 9-10).

Those skilled in the art appreciate the significance of homeostasis in the body, and understand that cell tissue is cast off (i.e. programmed cell death or "apoptosis") and regenerated, and adjustments in the balance between these processes in response to skin wounds will produce re-epithelization and healing. The inventors of the present invention disclose use of the rhamnolipids as beng "effective in re-epithelization of the skin" (page 7, lines 3-4). The primary focus of the evidence disclosed regarding re-epithelization is with the healing of wounds (pages 7-15), and there is no separate evidence with regard to signs of aging. However, one skilled in the art would understand that, to the extent that "signs of aging" is with reference to the skin, it is reasonable to conclude – as did the inventors – that if application of the

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rhamnolipids promotes re-epithelization, application of the rhamnolipids would thereby counter the effects of aging in the skin.

It should be emphasized that such a conclusion is not supported by the disclosures in Piljac '232 or Piljac '675. These disclosures, as described above, fail to describe or suggest the logic of the preceding paragraph. They are not adequate as §102 references because they do not discuss – or even suggest – a connection between signs of aging and the re-epithelization of skin tissue. The mere fact of topical application of rhamnolipids does not provide the necessary disclosure, except by improper hindsight.

The claims have been amended to clarify that “signs of aging” pertains to the skin, the application of rhamnolipids thereby promoting re-epithelization and thereby treating signs of aging of the skin.

The Examiner has rejected claims 26 and 28 under 35 U.S.C. §102(a) as being anticipated by U.S. Patent No. 4,902,512 to Ishigami. As with Piljac '232 and Piljac '675, the Examiner argues that topical application of rhamnolipid structures to adult skin anticipates the claimed method. For the same reasons discussed above, this argument can succeed only by improper hindsight. Furthermore, Ishigami uses the rhamnolipids to construct liposomes, for example to serve as drug carriers. It is not evident that liposomes constructed of rhamnolipids would have the same effect. In any event, the claims have been amended to more tightly link the application of the rhamnolipids to signs of aging of the skin and re-epithelization, which are neither described nor suggested by Ishigami.

In view of the foregoing, it is requested that the application be reconsidered, that claims 26-28 be allowed, and that the application be passed to issue.

Should the Examiner find the application to be other than in condition for allowance, the Examiner is requested to contact the undersigned at 703-787-9400